RAMAN-BASED GENE PROBE TECHNOLOGY

Dr. Vo-Dinh's nonradioactive, nonfluorescent gene probe is safe and sensitive.

Since the race to sequence the human genome began, about 20 percent of human genes have been at least partially sequenced. However, scientists have identified functions for only 3 percent of the postulated 80,000 to 100,000 genes.

BMDO HISTORY

With the help of funding through BMDO's Innovative Science and Technology Directorate and the Department of Energy, an advanced optical technology called surface-enhanced Raman optical data storage (SERODS) was born. Developed to greatly expand data storage capabilities beyond those achievable with conventional silicon technology, SERODS also spawned a novel gene probe technology, SERGen. SERGen requires no radioactive tags or special fluorescing dyes and cuts gene identification time drastically, from as many as 16 hours to a matter of minutes. It can also be used with conventional molecular biology techniques such as polymerase chain reaction.

HOW IT WORKS

Surface-enhanced Raman spectroscopy (SERS) is the basis for SERGen's ability to distinguish between single-stranded and double-stranded DNA. Adsorbing a gene sequence of interest onto an "enhancing" microstructured metal surface greatly strengthens the Raman signal, allowing a researcher to detect minute quantities of specific DNA sequences with a spectroscope. When a gene sequence of interest is introduced into the reaction, the SERS probe seeks out its complementary partner on the reaction plate; this process is known as hybridization. Hybridization indicates that a match has been made between two complementary strands of DNA. The double-stranded hybrids give a unique Raman signal, distinguishing them from the single-stranded, unmatched sequences.

MEDICAL SIGNIFICANCE

There are many areas in which SERGen would prove useful because of its rapidity and sensitivity. For example, in our era of increasing antibiotic resistance, SERGen may prove a boon to doctors who want to quickly identify resistant organisms. In this way, the proper medication can be prescribed and a wasted course of ineffective antibiotics can be avoided. There are many known resistance genes in bacteria. With a simple probe that represents the sequence of the resistance gene, SERGen can immediately identify this unique biochemical tag to narrow drug treatment choices.

SERGen has already been used in the laboratory to detect sequences from the genomes of HIV-1, hepatitis B, and *Mycobacterium tuberculosis* (the organism that causes tuberculosis). Therefore, SERGen can serve as a fast probe for diagnosing infections without the long wait for cultures or antibody assays.

A much more newsworthy application of SERGen is in the Human Genome Project, for which discussions are under way. Gene sequencing and identification timetables have accelerated impressively; however, these incremental improvements have been variations on a few themes of conventional molecular biology techniques. SERGen could offer a drastic improvement in methodology.

VENTURES OR PRODUCT AVAILABILITY

SERGen won a 1996 R&D 100 award, and a patent for the technology is pending.

CONTACT

Oak Ridge National Laboratory
Tuan Vo-Dinh, Ph.D.
P.O. Box 2008
Mail Stop 6101
Oak Ridge, TN 37831
Telephone: (423) 574-6249
Facsimile: (423) 576-7651
Email: tvo@ornl.gov
WWW: http://www.ornl.gov